Relationship of P Terminal Force V1 on Electrocardiogram with Left Atrial Function in Chronic Kidney Failure Patients on Hemodialysis

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ABSTRACT

Background: Chronic kidney failure is a worldwide public health problem.Cardiovascular disease is a common complication and the main cause of mortality in this population.Impaired left atrial function is an early marker of cardiovascular involvement and a prognostic factor that correlated with mortality in chronic kidney disease patients. We aim to investigate the relationship between P terminal force V1 (PTFV1), an ECG parameter, with left atrial function in chronic kidney failure patients on hemodialysis.
Method: This cross sectional study was done in chronic kidney failure patients on hemodialysis in Dr. Sardjito General Hospital Jogjakarta. Electrocardiogram and echocardiography were done after hemodialysis procedure. P terminal force V1 was measured by multiplying amplitude and duration of negative deflection of terminal P wave in V1. Abnormal PTFV1 was defined as PTFV1 value ≥ 40 mm.msec. Left atrial function was measured using left atrial peak global longitudinal strain (LA PGLS).
Results: This study was done in 71 patients with mean age 50 years old. Forty three subjects (61%) were men. Sixty four subjects (90%) had hypertension. Forty four subjects (62%) had abnormal PTFV1 on ECG. Mean LA PGLS was 24.89 ± 8.23%. No significant correlation was found between PTFV1 value with LA PGLS (r= -0.178; p=0.138). By multivariate analysis, left ventricular ejection fraction, left atrial diameter and hemodialysis duration (in months) were variables that independently correlated with LA PGLS. In subanalysis, amplitude of negative deflection of terminal P wave in V1 was significantly correlated with LA PGLS(r= -0.257, p= 0.031).
Conclusions: This study reveals no correlation between P terminal force V1 and left atrial function in chronic kidney failure patients on routine hemodialysis. There is significant correlation between amplitude of negative deflection of terminal P wave in V1 with LA PGLS.

Keywords: P Terminal Force V1; left atrial function; chronic kidney failure; hemodialysis

INTISARI

Latar belakang: Gagal ginjal kronis menjadi masalah kesehatan masyarakat di seluruh dunia. Penyakit kardiovaskular merupakan komplikasi tersering dan penyebab utama kematian pada populasi ini. Gangguan fungsi atrium kiri menjadi penanda awal penyakit kardiovaskular dan merupakan faktor prognostik kematian pada pasien penyakit ginjal kronis. Kami bertujuan untuk menyelidiki hubungan antara *P terminal force V1* (PTFV1), parameter EKG, dengan fungsi atrium kiri pada pasien gagal ginjal kronis yang menjalani hemodialisis.

Metode: Penelitian cross sectional ini dilakukan pada pasien gagal ginjal kronis yang menjalani hemodialisis di RSUP Dr. Sardjito Jogjakarta. Elektrokardiogram dan ekokardiografi dilakukan setelah prosedur hemodialisis. *P terminal force V1* diukur dengan mengalikan amplitudo dan durasi defleksi negatif dari gelombang terminal P di V1. *P terminal force V1* abnormal didefinisikan sebagai nilai PTFV1 ≥40 mm.msec. Fungsi atrium kiri diukur menggunakan atrial peak global longitudinal strain (LA PGLS).

Hasil: Penelitian ini dilakukan pada 71 pasien dengan usia rata-rata 50 tahun. Empat puluh tiga subjek (61%) adalah laki-laki. Enam puluh empat subjek (90%) memiliki hipertensi. Empat puluh empat subjek (62%) memiliki PTFV1 abnormal. Nilai rerata LA PGLS adalah 24,89 ± 8,23%. Tidak ada korelasi signifikan yang ditemukan antara nilai PTFV1 dengan LA PGLS (r =-0,178; p =0,138). Pada analisis multivariat, fraksi ejeksi ventrikel kiri, diameter atrium kiri dan durasi hemodialisis (dalam beberapa bulan) merupakan variabel yang secara independen berkorelasi dengan LA PGLS. Dalam subanalisis, amplitudo defleksi negatif dari gelombang P terminal di V1 secara signifikan berkorelasi dengan LA PGLS (r =-0,257, p =0,031).

Kesimpulan: Penelitian ini menunjukkan tidak ada korelasi antara kekuatan terminal P V1 dan fungsi atrium kiri pada pasien gagal ginjal kronis yang menjalani hemodialisis rutin. Terdapat korelasi yang signifikan antara amplitudo defleksi negatif dari gelombang P terminal di V1 dengan LA PGLS.

INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health problem.[1] The people with CKD have an increased cardiovascular risk.[2] Cardiovascular disease (CVD) is the most common complication in this population and has becoming the most common cause of mortality in terminal kidney disease, constituting 45-50% of all cause mortality.[3] In terminal kidney disease patients, mortality from CVD reaches 10-20 times higher than healthy population.[4] In this particular population, heart faces a chronic increased pressure and volume overload.[5]

An impaired left atrial (LA) function that is measured by echocardiography (left atrial peak global longitudinal strain/LA PGLS)has emerged as an early marker of cardiovascular involvement and prognostic factor that is correlated with mortality in CKD patients.[6-8] Echocardiography, especially with strain features, is scarce in rural areas. Meanwhile electrocardiography (ECG) is a cheap, easy to be used and available in rural districts.[9] A P terminal force V1 is an ECG parameter that has been studied and known to be correlated not only with LA size but also LA pressure and function.[10] This aim of this study is to know the correlation between PTFV1 on ECG and LA function in CKD patients on hemodialysis.

METHODS

This study was a cross sectional study. The subjects were CKD patients on routine hemodialysis (minimum already on hemodialysis for 3 months) in Dr. Sardjito General Hospital. The inclusion criteria were:CKD patients on routine hemodialysis, 18-75 years old, willing to participate on this study and signing the

informed consent. Exclusion criteria were: patients with atrial fibrillation, patients with severe primary heart valve disease, patients whose echocardiographic pictures difficult to be analyzed (in obtaining LA strain values). From 175 subjects on routine hemodialysis in Dr. Sardjito Hospital, 79 subjects fulfilled inclusion criteria, 8 subjects were excluded (5 subjects with atrial fibrillation and 3 subjects' echocardiographic pictures were unable to be analyzed). Finally there were 71 subjects that participated in this study.

Electrocardiogram (ECG) and echocardiography were done within 24 hours after hemodialysis procedure. A standard 12 leads ECG was done with ECG machine MAC 400 (General Electrics) and Cardisunny C110 (Fukuda M-E) with standard speed and callibration (25 mm/second and 10 mm/milivolt). The result was then scanned and read using Image J software. A P terminal force V1 was measured by multiplying duration and amplitude of negative deflection of terminal P wave in lead V1. Abnormal PTFV1 was defined as PTFV1 value ≥ 40 mm.msec.

Echocardiography was done with Vivid 7 and Cicid iq machine (General Electrics) by a trained echocardiographer. Standard echocardiography video was obtained, with particular attention to get good left atrium pictures (whole and not truncated) in apical four chamber and two chamber view. The video was then analyzed in work station with special software (Echo-Pac, General Electrics) to obtain LA PGLS with speckle tracking method. Peak value of left atrial global longitudinal strain curve at end systole (just before the mitral valve opening) was measured as LA PGLS. Normal value of LA PGLS is 39%.[11] The consistency ofPTFV1 and LA PGLS measurement (interobserver variability) was asessed by Cohen's kappa (K), if K >0.5 and p <0.05 measurement result was considered similar. This study had ethical approval from Medical and Health Research Ethics Commitee (MHREC) Faculty of Medicine, Public Health and Nursing Universitas Gadjah Mada, Jogjakarta, Indonesia.

Statistical analysis was done using SPSS software. Numerical data was presented as mean and standard deviation or median and minimum-maximum value. Categorical data was presented as proportion. Baseline characteristics and confounding factors were analyzed using bivariate analysis. The variables with $p < 0.25$ in bivariate analysis, was then analyzed using multivariat analysis. Correlation between PTFV1 and LA PGLS was measured using Pearson or Spearman correlation analysis. P value <0.05 was considered statistically significant.

RESULT

Of the 71 subjects, 43 were male (61%) and the mean age was 49.94±12.58 years (table 1). Mean systolic pressure was 138.85±25.19 mmHg, median diastolic pressure was 80 mmHg. Sixty four subjects (90.1%) had hypertension, 16 subjects (22.9%) was smoker or had previous history of smoking, 23 subjects (32.4%) had diabetes mellitus and 15 subjects (21.1%) had dyslipidemia. Forty four patients (62%) had abnormal PTFV1 on ECG. Mean amplitude of negative deflection of terminal P wave in V1 was 0.98±0.49 mm, mean duration of negative deflection of terminal P wave in V1 was 50.95±16.43 miliseconds. Median PTFV1 value was 44.16 (2.92-187.20) mm.ms.

Thirty two subjects (45%) had abnormal LAVI (>28 mL/m^2). Sixty two subjects (87%) had normal LVEF (> 50%). Fifty six subjects (71%) had abnormal LVMI. Sixty eight subjects (96%) had abnormal LA PGLS (table 1).

Normality test using Kolmogorov-Smirnov showed PTFV1 value data distribution was abnormal. Spearman analysis was used to analyse correlation between PTFV1 and LA PGLS. No correlation was found between PTFV1 and LA PGLS (r=-0.178; p=0.138). The scatter plot of this analysis is presented in figure 1.

Table 1. Baseline characteristics

Variables	Subjects (n=71)
Gender‡	
Male; n(%)	43 (61%)
Female; n(%)	28 (39%)
Age (years) †	49.94±12.58
Traditional risk factors‡	
Hypertension; n(%)	64 (90%)
Diabetes mellitus; n(%)	23 (32%)
Dyslipidemia; n(%)	15 (21%)
Smoking; n(%)	16 (23%)
Heart rate (times per minute) †	81.7±14.28
Systolic pressure (mmHg) †	138.85±25.19
Diastolic pressure (mmHg) ‡	80 (60-127)
Body mass index (kg/m^2) †	23.06±4.14
Hemodialysis duration (months) ‡	36 (3-192)
Medication use‡	
ACE inhibitor or ARB	60 (84%)
Calcium channel blocker	57 (80%)
Beta blocker	5 (7%)
Abnormal PTFV1‡	44 (62%)
Amplitude of negative deflection of terminal P wave in V1 (mm) †	0.98±0.49
Duration of negative deflection of terminal P wave in V1 (ms) †	50.95±16.43
PTFV1 value (mm.ms) ‡	44.16 (2.92-187.20)
LVIDd ‡	48.00 (34.00-69.00)
LVMI ‡	144.61 (68.6-338.5)
Abnormal LVMI‡	56 (71%)
Left ventricular ejection fraction (LVEF)‡	69 (20.0-83.0)
Normal LVEF(> 50%)	62 (87%)
Left ventricular wall motion‡	
Normokinetic	59 (83%)
Wall motion abnormality	12 (17%)
Left ventricular diastolic function‡	
Normal	44 (62%)
Diastolic dysfunction	17 (24%)
Indeterminate	10 (14%)
LA diameter†	38.03±5.78
LAVI ‡	27 (5.0-72.63)
Abnormal LAVI (> 28 mL/m^2)	32 (45%)
LA PGLS†	24.89 ± 8.23
Abnormal LA PGLS (< 39%)‡	68 (96%)

PTFV1: P terminal force V1; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker, LVIDd: left ventricular internal diastolic diameter; LVMI: left ventricular mass index;LA: left atrium; LAVI: left atrial volume index; PGLS: peak global longitudinal strain.

‡ data was presented as percentage

†normal data distribution, data was presented as mean and standard deviation

‡abnormal data distribution, data was presented as median, minimum and maximum value

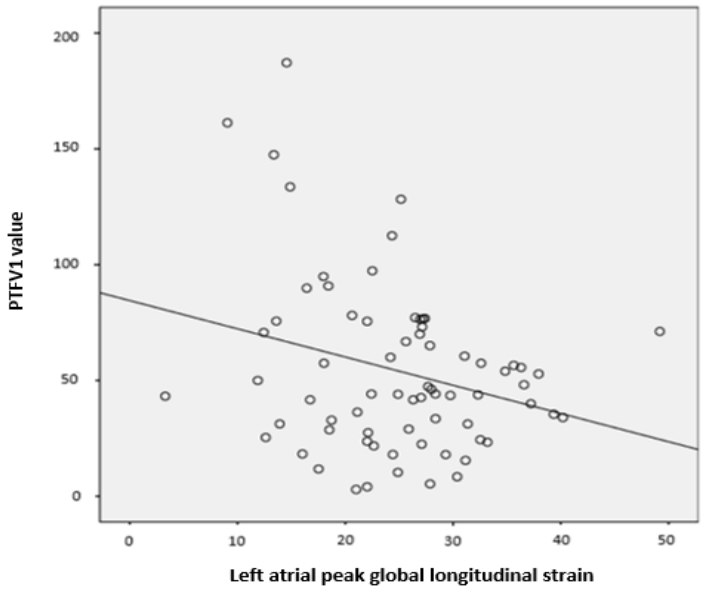

Figure 1.Scatter plot of PTFV1 value with LA PGLS in CKD undergoing hemodialysis population (r =-0.178; p =0.138).

Table 2. Bivariate analysis of LA PGLS and confounding factors

Confounding factors	r	p
Age †	-0.012	0.924
Hemodialysis duration ‡	0.181	0.130
LA diameter †	-0.481	0.000*
LAVI ‡	-0.345	0.003*
LVIDd ‡	-0.370	0.001*
LVMI ‡	-0.289	0.015*
LVEF ‡	0.447	0.000*
Amplitude of negative deflection of terminal P wave in lead V1 †	-0.257	0.031*

LVIDd: left ventricular internal diastolic diameter; LVMI: left ventricular mass index; LAVI: left atrial volume index; LA: left atrium; LVEF: left ventricular ejection fraction

†normal data distribution, ‡abnormal data distribution,

*data with significant value

Further analysis was done for LA PGLS and the confounding factors. The confounding foctors are age, hemodialysis duration, LA diameter, LAVI, LVIDd, LVMI, LVEF, amplitude of negative deflection of terminal P wave in lead V1, diabetes mellitus, hypertension, LV diastolic dysfunction and medication usage (ACE inhibitor or ARB, CCB, beta blocker). Bivariate analysis between LA PGLS and the confounding factors is presented in table 2, meanwhile LA PGLS value mean difference among the confounding factors is presented in table 3.

Table 3. LA PGLS mean difference among the confounding factors

Confounding factors	Yes	No	p
Diabetes mellitus	22.23±5.94 (n=23)	26.16±8.89 (n=48)	0.058
Hypertension	25.14±8.50 (n= 64)	22.61±4.89 (n= 7)	0.444
Diastolic dysfunction	18.41±6.44 (n= 17)	27.76±7.95 (n= 44)	0.000*
ACE inhibitor/ARB	24.27±7.83 (n=60)	28.27±9.83 (n=11)	0.139
CCB	24.97±7.78 (n=57)	24.54±10.15 (n=14)	0.862
Beta blocker	22.33±10.02 (n= 5)	28.27±9.83 (n= 11)	0.475

ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; CCB: calcium channel blocker

* data with significant value

Table 4. Multivariate analysis of LA PGLS and the confounding factors

Confounding factors	r	P
LVEF	0.450	0.005*
LA diameter	-0.325	0.030*
Hemodialysis duration	0.247	0.037*
LVIDd	0.197	0.277
ACE inhibitor / ARB	-0.114	0.326
Diabetes mellitus	0.107	0.337
LVMI	-0.064	0.650
LV diastolic disfunction	-0.056	0.634
LAVI	-0.012	0.938
Amplitude of negative deflection of terminal P wave in lead V1	-0.058	0.597

LVIDd:left ventricular internal diastolic diameter; LVMI: left ventricular mass index;LAVI: left atrial volume index; LA: left atrium; LVEF: left ventricular ejection fraction; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker

*data with significant value

Confounding factors with p <0.25 was then included in multivariate analysis. Based on the multivariate analysis, LVEF, LA diameter and hemodialysis duration were independently associated with LA PGLS (table 4).

Furthermore, a subanalysis was doneto see the correlation between PTFV1 components (duration and amplitude of negative deflection of terminal P wave in lead V1) with LA PGLS. Components of PTFV1 had normal data distribution (analyzed using Kolmogorov-Smirnov), correlation analysis was done using Pearson analysis.

Correlation analysis between duration of negative deflection of terminal P wave in lead V1 and LA PGLS using

Pearson showed a negative correlation with r =-0.112, but this association is not significant (p =0.351). Meanwhile correlation analysis between amplitude of negative deflection of terminal P wave in lead V1 and LA PGLS using Pearson showed a significant negative correlation with r =-0.257 (p = 0.031). The result is presented in table 5 and the scatter plot is showed in figure 2. In linear regression test it was found that each 1 mm increase in the depth of negative deflection of terminal P wave in lead V1 will decrease LA PGLS value of 4.34% (p =0.031).

Table 5.Correlation of P terminal force V1 components with LA PGLS

P Terminal Force V1 components	r	p
Amplitude of negative deflection of terminal P wave in V1 (mm)	-0.257	0.031*
Durationof negative deflection of terminal P wave in V1 (milidetik)	-0.112	0.351

LA PGLS: left atrial peak global longitudinal strain
*data with significant value

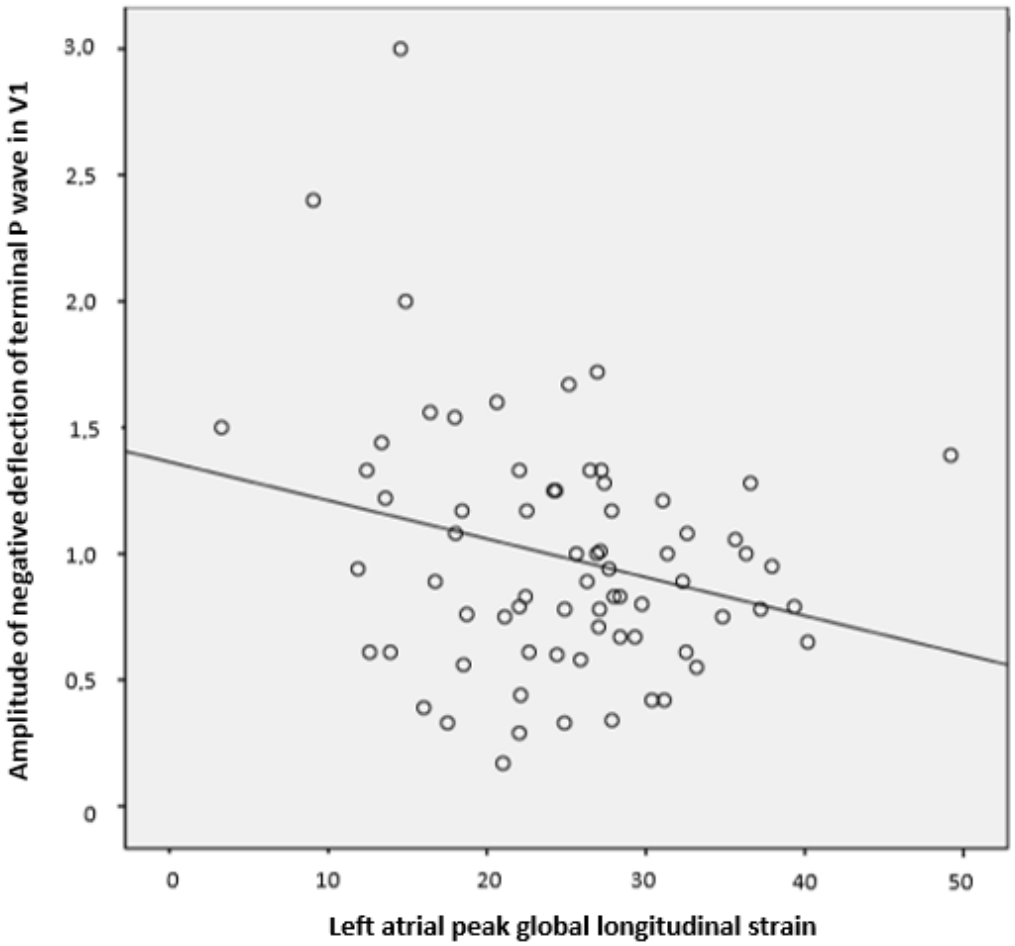

Figure2. Scatter plotdepicting correlation between amplitude of negative deflection of terminal P wave in V1 and LA PGLS (r = -0.257, p <0.05).

DISCUSSION

Abnormal PTFV1 was found in 44 subjects (62%) out of total 71 subjects in this study. This is consistent with previous finding, that abnormal PTFV1 was found in 66% patients on routine hemodialysis.[10] Prevalence of abnormal PTFV1 in hemodialysis population is higher than in normal population (7,5%).[12] This is because there is increased LA size in terminal kidney disease population that's happened because pressure and volume overload and high prevalence of LV diastolic dysfunction in this population.[13,14]

Mean LA PGLS in this study is 24.89±8.23%, lower than normal value from meta analisis by Pathan *et al*. (39%). This is consistent with previous findings in CKD patients that showed decreased LA PGLS value i.e 25.7±9.3% dan 28.8±14,.9%.[15,16] These showed that there is impaired LA function in CKD patients, this can be caused by an increased pressure and volume overload in this population that finally cause LA remodelling.[14,17]

In this study, PTFV1 value is not correlated with LA PGLS. This is different with previous study that showed significant correlation between PTFV1 and LA function in hemodialysis patients.[11] The difference might be caused by different hemodialysis characteristics related with fluid overload, i.e in previous study, hemodialysis was done three times a week and in this study hemodialysis was done twice a week. This can influence body's volume status. When LA is overloaded, P wave vector will rotate to the left and posterior, causing prominent negative component of P wave in V1.[18]

From multivariate analysis it is found that LA diameter, LVEF and hemodialysis duration are factors that independently associated with LA PGLS. Left atrial PGLS resembles LA reservoir function.[19] From previous study, it is found that LA reservoir function consists of early and late phase. Early reservoir function depends on LA relaxation meanwhile late reservoir function depends on LV contraction (descent of LV base) at systole.[20] This can explain why LVEF independently associated with LA PGLS.

An LA dilatation is the hallmark of LA structural remodelling. Increased pressure or volume overload can increase LA size, but pressure overload usually accompanied by abnormal myocyte relaxation, meanwhile in volume overload, myocyte relaxation usually normal.[21] In CKD, LA not only face increased volume overload but also pressure overload (because of hypertension and LV diastolic dysfunction).[14] Impaired atrial relaxation surely will impair LA reservoir function measured by LA PGLS.

Hemodialysis duration is associated independently with LA PGLS (r = 0,247; p = 0,037). Hemodialysis itself can cause ischemia, injury and impaired myocardial function because non physiologic fluid removal and decreased intradialytic myocardial perfusion.[22] Repeated interdialytic fluid retention also contributed to LV hyperthrophy, LV diastolic dysfunction and finally LA remodelling.[14,23] But as the patients getting used to hemodialysis, they were exposed to essential information such as the importance of fluid control and routine consumption of medication. Discipline fluid restriction will produce optimal interdialytic weight gain so that cardiac load can be controlled well.[24] Good colume control and antiremodelling medication can help reverse remodelling to happen and this can repair LA size and function.[17,25]

Duration of negative deflection of terminal P wave in V1 is not associated with LA PGLS (r = -0.112, p = 0.351), but amplitude of of negative deflection of terminal P wave in V1 significantly associated with LA PGLS (r= -0.257, p = 0.031). This is consistent with previous findings that there is no correlation between duration of negative deflection of terminal P wave in V1 and LA PGLS, meanwhile amplitude of negative deflection of terminal P wave in V1 was correlated significantly with LA strain, i.e

for each increase 0,1 mV in the depth of negative deflection of terminal P wave in V1 is associated with LA strain decrease 7,5% (p = 0.037).[18]

Duration of negative deflection of terminal P wave in V1 represents time/duration of impulse conduction in LA. This represents impaired conduction in atrium or LA dilatation so that impuls need more time to finish the conduction in the whole LA.[18,26] Meanwhile amplitude of negative deflection of terminal P wave in V1 represents LA wall hyperthrophy. Loewe et al. with an in silico LA model found that LA wall thickness was strongly correlated with amplitude of of negative deflection of terminal P wave in V1, but P wave duration was almost not influenced by LA wall thickness.[27] This anatomical changes (LA wall hyperthrophy) can influence myocyte relaxation function.[17,21] The impaired function is caused by functional remodelling that cause contractile protein isoform composition changes that finally cause impaired relaxation of myocytes.[28,29]

Limitations

This research did not study LA conduit and contractile strain. Parameter in hemodialysis i.e ultrafiltration rate and volume was not taken and analyzed in this research.

CONCLUSIONS

This study reveals no correlation between P terminal force V1 and left atrial function measured with left atrial peak global longitudinal strain in chronic kidney failure patients on routine hemodialysis. There is significant correlation between amplitude of negative deflection of terminal P wave in V1 with LA PGLS.

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